

Remarks

Claims 1, 12, 14-18, 27, 41-44, and 54-61 were pending in the application. No claims are cancelled or added, therefore, **claims 1, 12, 14-18, 27, 41-44, and 54-61** remain pending in this application. Consideration of the pending claims is requested.

Claims 1, 27, and 56 are amended herein. No new matter is added. Support for the claim amendments can be found in the specification, for instance at page 7, line 32 to page 8, line 3; page 11, lines 15-21; page 8, lines 27-29; page 2, lines 23-33; and page 9, lines 29-34.

Applicants thank the Examiner for withdrawing the previous rejection of claims 1, 12, 14-18, 41-44, and 55 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Applicants note that claim 54 was also previously included in this rejection and request clarification as to the status of this claim.

Claim Rejections – 35 U.S.C. § 112

Written Description

Claims 1, 12, 14-18, 27, 41-44, and 55-61 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Applicants request reconsideration.

The Office asserts that the application does not provide “support for the specifically claimed steps because there is no description of the combined method steps of claim 1 or any description of assaying the Axl kinase activity for identifying compounds that inhibit angiogenesis” (Office action, page 7, paragraph 1). Applicants disagree. Applicants assert that a literal description of the combined method steps is not required to provide adequate written description for the pending claims. Further, Applicants point out that the specification specifically describes use of Axl kinase activity to identify compounds that inhibit angiogenesis.

To establish a *prima facie* case of lack of written description, the Office must provide “reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the

disclosure of the application as filed.” MPEP § 2163.04(I)(B). The Office has not met this *prima facie* burden. There is no requirement that the specification explicitly describe every aspect of the claims to provide adequate written description. As established in *Ex parte Parks*, “adequate description under the first paragraph of 35 U.S.C. 112 does not require literal support for the claimed invention... Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed.” *Ex parte Parks*, 30 USPQ2d 1234, 1236 (BPAI 1993) (emphasis added). Moreover, the MPEP at § 2163 states “[w]hat is conventional or well known to one of skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94... If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g. *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating “description need not be in *ipsis verbis* [i.e., “in the same words”] to be sufficient”).”

Applicants assert that a literal description of the combination of two assays for identifying inhibitors of angiogenesis (as in claim 1) is *not* required, and even if it is, that the specification provides adequate support for such a combination. The Office acknowledges that the specification provides support for “Axl, its ligands, expression, and association with diseases..., a general description of an assay to identify inhibitors of angiogenesis/tumorigenesis ..., the definition of ‘functional effect’..., numerous assays to measure angiogenesis... In one embodiment measurement of integrin cell surface expression is used to identify modulators of angiogenesis ..., measuring ligand binding, cell surface marker expression, cellular proliferation, VEGF-R assays, co-culture assays for tube formation..., haptotaxis..., CAM assays, cellular morphology..., kinase activity..., treatment of HUVEC cells with RNAi directed to Axl inhibits the haptotaxis, proliferation, and tube formation in HUVEC cells...” (Office action, paragraph bridging pages 3 to 4). Applicants agree that the application clearly supports use of these (and other) assays, including Axl kinase activity and cell-based angiogenesis phenotype, to identify inhibitors of angiogenesis.

In addition to support in the specification for the individual assays set out in claims 1, 27, and 56, support for the present claims is also found in original claim 1. Original claim 1 recited “a method for identifying a compound that modulates angiogenesis, the method **comprising** the steps of: (i) contacting the compound with an angiogenesis polypeptide...; and (ii) determining the functional effect of the compound upon the angiogenesis polypeptide...” (emphasis added). This claim includes determining a functional effect on Axl; the specification defines determining a functional effect as “assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of an angiogenesis protein...” (specification, page 8, lines 27-29). The specification goes on to describes assays for measuring such functional effects as including “measuring changes in enzymatic activity; the ability to increase or decrease cellular proliferation, apoptosis, cell cycle arrest, measuring changes in cell surface markers... Determination of the functional effect can also be performed using assays... such as endothelial cell tube formation assays; haptotaxis assays; the chick CAM assay; the mouse corneal assay; VEGF receptor assays, co-culture tube formation assays, and assays that assess vascularization of an implanted tumor” (specification page 8, line 34 to page 9, line 8). Original claim 1 thus encompassed assaying any functional effect described by the specification. There is no indication in the specification that only one functional assay could be used to identify an inhibitor of angiogenesis. Amended claim 1 (and claims 27 and 56) merely explicitly set forth specific functional effects (kinase activity and cell-based angiogenesis phenotype) that can be used to identify inhibitors of angiogenesis. As these specific functional effects are supported by the specification (as acknowledged by the Office), a method that utilizes assaying more than one of these functional effects is also supported by the specification, particularly as the original claims recited the open transition phrase “comprising.” “The transition ‘comprising’ in a method claim indicates that the claim is open-ended and allows for additional steps.” *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003).

Applicants also reassert the previous argument that one of skill in the art would readily recognize from the specification that any combination of the described assays could be used in methods for identifying compounds that inhibit angiogenesis. The specification describes the use of combinations of other assays of functional effects, such as the use of a combination of assays in Figure 13 (effect of Axl RNAi on haptotaxis and $\beta 1$ integrin expression) and Figure 15

(effect of Axl RNAi on haptotaxis and cell proliferation). Based on the description of combinations of assays in the specification, one of skill in the art would clearly recognize from the specification that Applicants had possession of the claimed subject matter at the time of filing of the application.

With regard to the alleged lack of description of assaying Axl kinase activity to identify inhibitors of angiogenesis, the specification clearly describes determining Axl kinase activity to identify angiogenesis inhibitors. As a preliminary matter, Axl was well known at the time of filing of the application as a receptor tyrosine kinase (see, *e.g.*, page 6, lines 9-11). The specification describes assaying for a compound that modulates angiogenesis by determining “a parameter that that is indirectly or directly under the influence of an angiogenesis polypeptide” (page 8, lines 15-18). Axl is defined by the specification as an angiogenesis polypeptide (see, *e.g.*, page 5, lines 22-23 and page 6, lines 8-9). Without more, one of skill in the art would clearly recognize that Axl kinase activity is a parameter under the influence of Axl. However, the specification further describes the parameters that are to be assayed to include enzymatic activity (see, *e.g.*, page 8, line 22; page 8 line 34 to page 9, line 1; page 31, lines 26-27). Further, *the Office acknowledges* that the specification supports use of kinase activity to identify modulators of angiogenesis (Office action, page 4, line 8). Therefore, one of skill in the art would certainly recognize that assaying Axl kinase activity for identifying inhibitors of angiogenesis was in possession of the inventors at the time of filing.

The Office also asserts that the application does not provide support for “an Axl polypeptide with ‘greater than’ 95% identity to full length SEQ ID NO: 4, only ‘greater than about’ 95% identity” (Office action, page 4, last paragraph). Applicants disagree. Moreover, Applicants note that a polypeptide with greater than 95% identity would fall within the broader genus of a polypeptide having greater than *about* 95% identity, and thus is supported by the specification. A genus encompasses a collection of elements and is analogous to a range, while a subgenus is a narrower subset of the elements of the genus and is analogous to a narrower range within a broader range. When Applicants “clearly claim a range *within* the described [] range... the question is whether, *on the facts*, the PTO has presented sufficient reason to doubt that the broader described range also describes the somewhat narrower claimed range.” *In re Wertheim*,

191 USPQ 90, 98 (CCPA 1976) (emphasis in original). Applicants assert that the Office has not provided any reasoning as to why the broader genus (“greater than about 95% identity”) does not also describe the narrower subgenus (“greater than 95% identity”). In the current case, as in *In re Wertheim*, “[t]he PTO has done nothing more than to argue lack of literal support, which is not enough” (191 USPQ at 98). Nonetheless, to expedite prosecution, Applicants herein amend claims 1, 27, and 56 to recite “an amino acid sequence with greater than *about* 95% identity to full length SEQ ID NO: 4...,” as suggested by Examiner Reddig. Support for this amendment may be found in the specification, for example at page 7, line 32 to page 8, line 3 and page 11, lines 15-21. This has already been acknowledged by the Examiner.

Finally, the Office asserts that the application does not support “an Axl polypeptide comprising SEQ ID NO: 4 which encompasses sequences outside of SEQ ID NO: 4” (Office action, page 4, last paragraph). The Written Description Training Materials (Revision 1, March 25, 2008) in Example 4A discusses the effect of open transitional language, such as that of the present claims. Example 4A describes a specification disclosing SEQ ID NO: 16 and a claim reciting “an isolated DNA comprising SEQ ID NO: 16.” The training materials indicate that although the sequence could be combined with other sequences, “the scope of the genus is defined by the presence of the structure shown in SEQ ID NO: 16. Thus all members of the genus will predictably include SEQ ID NO: 16... Because SEQ ID NO: 16 is a structural feature common to all members of the genus and the specification describes the complete structure (sequence) of SEQ ID NO: 16, one skilled in the art would recognize that the applicant was in possession of a common structural feature of members of the genus.” The example goes on to conclude that the specification satisfies the written description requirement with respect to this claim. The present situation is directly analogous to Example 4A. Applicants’ specification discloses the amino acid sequence SEQ ID NO: 4 and the claims recite “an Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4...” Therefore, the specification provides adequate written description for an Axl polypeptide including the structure shown in SEQ ID NO: 4 (or with greater than about 95% identity to full length SEQ ID NO: 4) even in combination with additional sequences attached to either end of SEQ ID NO: 4.

Based on the foregoing amendments and arguments, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, written description.

Indefiniteness

Claims 1, 12, and 14-18 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants request reconsideration.

Claims 1, 12, and 14-18 are rejected as indefinite for omitting the allegedly essential step of “contacting the Axl polypeptide or cell comprising the Axl polypeptide with the compound being examined” (Office action, page 9). Applicants first point out that “a claim which omits matter disclosed to be essential to the invention as described in the specification...may be rejected under 35 U.S.C. § 112, first paragraph *as not enabling*.” MPEP § 2172.01, emphasis added (citing *In re Mayhew*, 527 F.2d 1229 (CCPA 1976)). Therefore, this rejection is not properly raised under 35 U.S.C. § 112, second paragraph.

Even if this rejection were properly made, the proper standard must be applied. “Determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.” *Solomon v. Kimberly-Clark Corporation* 216 F.3d 1372, 1378 (Fed. Cir. 2000). Further, “[t]he requirement to ‘distinctly’ claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles... Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite.” *Metabolite Labs, Inc. v. Lab Corp. of Am. Holdings* 370 F.3d 1354, 1366 (Fed. Cir. 2004).

Applicants assert the claims have a discernible meaning to one of skill in the art and are therefore definite. However, solely to advance prosecution, claim 1 is amended herein to recite “assaying *in vitro* kinase activity of an Axl polypeptide comprising an amino acid sequence with greater than about 95% identity to full length SEQ ID NO: 4 *in the presence of the compound*,

wherein the Axl polypeptide has kinase activity in the absence of said compound; and performing a cell-based assay in an endothelial cell comprising said Axl polypeptide *in the presence of the compound*, which assay produces an angiogenesis phenotype in said endothelial cell in the absence of the compound...” Support for this amendment may be found in the specification, for example at page 2, lines 23-33; page 9, lines 29-34. The amended claims have a clearly discernible meaning to one of skill in the art and do not omit essential matter (that is, they are enabled) nor fail to interrelate essential elements of the invention (that is, they are definite). Further, claim 1 recites “wherein inhibition of the *in vitro* kinase activity of the Axl polypeptide in the presence of the compound and inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis” (emphasis added).

Claim 1 as amended sets forth that the assay is to be performed in the presence of a test compound. Further, the specification sets forth that “samples or assays comprising angiogenesis or tumorigenesis proteins that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition” (page 9, lines 32-34). Therefore, when claim 1 is read in light of the specification, one of skill in the art would readily understand that the assays are performed in the presence of the compound. It is not essential that the claim recite a step of contacting the Axl polypeptide or the cell comprising the Axl polypeptide with the compound. Based on the foregoing amendment and arguments, claim 1 clearly sets forth the metes and bounds of the claim and apprises one of skill in the art of the scope of the invention. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claim Rejections – 35 U.S.C. § 102

Claims 1, 14, 27, 54-56, and 61 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Healy *et al.* (*Am. J. Physiol. Lung Cell Mol. Physiol.* 280:L1273-L1281, 2001). Applicants traverse.

The Office alleges that Healy *et al.* teach “determining the *in vitro* kinase activity of an Axl polypeptide...[,] performing a cell-based assay in an endothelial cell... and determining the

effect of this interaction on cell number...” as well as teaching assaying apoptosis in endothelial cells expressing Axl (Office action, page 10, second paragraph). The Office further asserts that as Healy allegedly “comprises the same method steps as claimed in the instant invention, determining *in vitro* kinase activity of an Axl polypeptide...; and performing a cell based assay in an endothelial cell comprising said Axl polypeptide... the claimed method is anticipated because the method will *inherently* be a method for identifying a compound that inhibits angiogenesis...” (Office action, paragraph bridging pages 10-11, emphasis added).

A rejection under 35 U.S.C. § 102 is appropriate “only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference.” MPEP § 2131. However, “[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic ... Inherency, however, may not be established by probabilities or possibilities.” MPEP § 2112. In order to show inherency, a gap in a reference may be filled by extrinsic evidence, but the “evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.” *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991); MPEP § 2131.01, emphasis added. Applicants strongly assert that Healy *et al.* does not inherently anticipate the claimed methods and the Office has not provided any extrinsic evidence to make clear that Healy *et al.* necessarily does so.

As a preliminary matter, Applicants point out that Healy *et al.* teach that contacting human pulmonary artery endothelial cells (HPAEC), which express Axl polypeptide, with exogenous Gas 6 (an Axl ligand) increased Axl phosphorylation (page L1276, column 2 and Figure 5). Healy *et al.* also teach that contacting the HPAEC cells with Gas 6 increased cell number (page L1276, column 2 and Figure 6). Finally, Healy *et al.* teach that contacting the HPAEC cells, or HPAEC cells overexpressing Axl, with Gas 6 decreased apoptosis of the cells in serum free medium (page L1277, column 2; page 1278, column 2; Figures 8 and 10).

Healy *et al.* do not teach that Gas 6 is an angiogenesis inhibitor. This has been previously noted by Applicants (Office action response of February 23, 2007, page 15, third

paragraph). This has also been *admitted by the Office*, which stated “Healy does not teach that Gas 6 specifically inhibits angiogenesis...” (Office action of May 7, 2007, page 11, third paragraph), when this rejection was last withdrawn. In the Office action of May 7, 2007, the Office attempted to cure the deficiencies of Healy *et al.* by asserting that Gallicchio *et al.* (*Blood* 105:1970-1976, 2005; cited in the Office action of May 7, 2007) provides evidence that Gas 6 inhibits angiogenesis upon interacting with Axl (Office action of May 7, 2007, page 12, first paragraph).

Healy *et al.* teach determining only the effect of Gas 6 on Axl polypeptide kinase activity and cell proliferation and apoptosis of cells expressing Axl polypeptide. Gas 6 *stimulates* Axl polypeptide activity, which inhibits activation of vascular endothelial growth factor receptor 2 (VEGFR2) and leads to *inhibition* of an angiogenic program in vascular endothelial cells (Gallicchio *et al.*, abstract; page 1973, first full paragraph; Figure 4A). Based on Gallicchio *et al.*, one of skill in the art would predict that *inhibition* of Axl polypeptide activity would *stimulate* activation of an angiogenic program in vascular endothelial cells. Thus, the expected effect of Healy *et al.* would be the *opposite* of Applicants’ demonstrated inhibition of angiogenesis. As Gas 6 is neither an inhibitor of Axl nor an inhibitor of angiogenesis, Healy *et al.* do not expressly or inherently teach a method of identifying a compound that is an inhibitor of angiogenesis and therefore this reference does not anticipate the claims.

Applicants point out that the foregoing discussion was previously presented in the amendment of October 5, 2007 and it was tacitly acknowledged and accepted as persuasive by the Office, which withdrew this rejection without comment in the Office action of December 12, 2007. Applicants emphasize that this rejection under 35 U.S.C. § 102(b) has previously been overcome and that Healy *et al.* still does not anticipate the claims.

Applicants further point out that claim 1 requires assaying *in vitro* kinase activity of an Axl polypeptide *and* performing a cell-based assay in an endothelial cell comprising said Axl polypeptide. In contrast, Healy *et al.* do not teach performing *both* of these assays in order to identify an inhibitor of angiogenesis. Thus, Healy *et al.* clearly does not anticipate claim 1 and its dependent claims.

Finally, the Office states that “‘determining the functional effects of the compound upon the kinase activity of the Axl polypeptide,’ when given its broadest reasonable interpretation encompasses assaying cellular responses such as increases or decreases in cellular proliferation and apoptosis” (Office action, page 10, third paragraph). Applicants point out that this language (“determining the functional effect”) is no longer present in claims 1 or 27. This language was removed from claim 1 in the amendment of October 5, 2007 and from claim 27 in the amendment of March 12, 2008. Further, Applicants assert that this is an unreasonably broad interpretation of claim 56. As discussed above, the specification defines “determining a functional effect,” which includes assaying kinase activity. However, claim 56 does not recite “determining a functional effect.” Claim 56 recites “determining a functional effect of the compound *upon the kinase activity* of the Axl polypeptide.” This claim cannot reasonably be interpreted as including determination of *any* functional effect; a proper interpretation is determining the effect of a compound on the kinase activity of the Axl polypeptide. However, solely in the interest of expediting prosecution, claim 56 is amended herein to recite “assaying the kinase activity of the Axl polypeptide.” Healy *et al.* teach only assaying the effect of Gas 6 on Axl kinase activity. As discussed above, Gas 6 is neither an inhibitor of Axl nor an inhibitor of angiogenesis. Thus, Healy *et al.* do not expressly or inherently teach a method of identifying a compound that is an inhibitor of angiogenesis and this reference does not anticipate the claims.

Based on the foregoing, Applicants request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Claim Rejections – 35 U.S.C. § 103

Claims 12, 15-18, 41-44, and 57-60 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Healy *et al.* in view of Varner and Cheresch (*Curr. Opin. Cell Biol.* 8:724-730, 1996), in further view of Ruoslahti *et al.* (U.S. Pat. No. 6,180,084), in further view of Panzer *et al.* (U.S. Pat. Application No. 2004/0048253), and in further view of Klinghoffer *et al.* (U.S. Pat. Application No. 2004/0077574). Applicants request reconsideration.

In order to establish a *prima facie* case of obviousness, the Office must establish that (1) there is some suggestion or motivation to combine the references, either in the references or in common general knowledge of one of skill in the art (MPEP § 2143.01); and (2) there is a reasonable expectation of success (MPEP § 2143.02). In addition, the Office must show that the references teach or suggest all claim limitations. “When determining whether a claim is obvious, an Examiner must make ‘a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.’ Thus, ‘obviousness requires a suggestion of all limitations in a claim.’” *Ex parte Mumper* BPAI, Appeal No. 2008-2332, June 27, 2008. Claims 12, 15-18, 41-44, and 57-60 depend from claim 1, 27, or 56.

Based on the discussion of Healy *et al.* above, Applicants maintain that Healy *et al.* do not teach all the limitations of the claims, namely that Healy *et al.* do not teach or even suggest identification of an inhibitor of angiogenesis. Further, Healy *et al.* make no suggestion that Axl polypeptide plays a role in angiogenesis. Rather, Healy *et al.* teach only that Axl and its ligand Gas 6 have anti-apoptotic activity in HPAEC cells and that this may be “relevant to endothelial cell survival in the quiescent environment of the vessel wall” (Healy *et al.*, abstract).

The Office action alleges that Varner and Cheresch teach a role for integrin $\alpha v \beta 3$ in angiogenesis. However, Varner and Cheresch do not teach or suggest a role for Axl polypeptide in angiogenesis nor selecting a compound that inhibits *in vitro* kinase activity of Axl polypeptide and inhibits angiogenesis phenotype in a cell-based assay to identify inhibitors of angiogenesis. Therefore, this reference does not cure the deficiencies of Healy *et al.* Likewise, Panzer *et al.* and Ruoslahti *et al.* teach only general methods of screening small molecules and other compounds for use in diagnosis or therapy. There is no discussion of Axl polypeptide in these references; therefore they cannot cure the deficiencies of Healy *et al.* Klinghoffer *et al.* teach only use of siRNAs for altering gene expression. This reference discloses Axl only as containing a potential protein tyrosine phosphatase 1B recognition motif (Klinghoffer *et al.*, paragraph [0016]) and does not teach or suggest a role for Axl polypeptide in angiogenesis. Therefore Klinghoffer *et al.* cannot be used to cure the deficiencies of Healy *et al.*

The Office does not provide any rationale for one of skill in the art to combine or modify the cited references. Taken together, one of skill might be motivated to assay regulation of apoptosis by Axl, not regulation of angiogenesis. However, the claims are based on the novel recognition that inhibition of Axl polypeptide inhibits angiogenesis. None of the cited references disclose that Axl has any role in angiogenesis, nor suggest that inhibitors of Axl could be inhibitors of angiogenesis. Without the recognition that inhibition of Axl inhibits angiogenesis, there is no motivation to combine the references and no expectation of success in arriving at the claimed invention by combining the references. Thus, alone or in combination, the cited references do not support a *prima facie* case of obviousness.

In sum, none of the references cited by the Office teach or suggest, either alone or in combination, all of the features of Applicants' claims. It remains well-settled law that obviousness requires at least a suggestion of all of the features in a claim. *See Ex parte Mumper* (BPAI, Appeal 2008-2332, June 27, 2008) citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). The Office has not met this burden and has not provided any "*articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex*, 127 S. Ct. 1727, 1741 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants respectfully request entry of this amendment. The Examiner is requested to contact the undersigned to arrange a telephonic interview prior to the preparation of any further written action.

Respectfully submitted,

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